REMARKS

Status of the Application

Claims 1-29 were originally filed in this application. The Office withdrew claims 3-29. Applicants herein amend claim 1 and present new claims 30-36. The new claims all depend from claim 1 and are drawn to nucleic acid sequences. Thus, they should be grouped with claims 1 and 2 for purposes of examination. Thus, claims 1-36 are now pending, and of those claims, claims 1-2 and 30-36 are under examination.

The amendment to claim 1 clarifies the location of the mutated nucleotides in the overall sequence, and is supported in the application as a whole, for example, by SEQ ID NO:1. Claim 1 is also amended to recite that the "polynucleotide encodes a polypeptide with FSAP activity." This amendment is also supported by the application as a whole, for example, in Table 1, at page 4. New claims 30-36 are also supported by the application as a whole, *inter alia*, at Table 1, at page 4; page 6, lines 1-14 and Table 2; and SEQ ID NOS:1-4.

Applicants also present a replacement abstract in order to remove the title and headers that were on the same page as the originally filed abstract.

Applicants respectfully request the entry of these amendments.

Objection to the Specification

The Office objects to the specification because the abstract as originally filed included the header "AVENTIS BEHRING GMBH 2000/A008-A7." (Office Action at page 4.) Applicants herein submit a replacement abstract. Applicants also provide some minor amendments to the grammatical form of the abstract.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

Rejection under 35 U.S.C. § 112, First Paragraph, Written Description

The Office rejects claim 1, alleging insufficient written description support. (Office Action at page 4.) Applicants traverse this rejection.

First, Applicants note that claim 1 is amended to recite that the claimed "polynucleotide encodes a polypeptide with FSAP activity." This condition also applies to claims 2 and 30-36, which depend from claim 1. Therefore, Applicants have provided appropriate structure/function correlation to characterize this genus.

Second, members of the instant claimed genus are described in Tables 1 and 2 at pages 4-6 of the application. These members are FSAP polynucleotides that were isolated and purified from patient samples and for which FSAP activity was screened by examining the ability of the FSAP mutant species to activate prourokinase. Some of the isolates showed reduced FSAP activity, corresponding to new claim 36, for example. (Specification at Tables 1 and 2.)

Third, the genus of claims 30 and 36, for example, are further limited either structurally or functionally. In addition, the genus described by new claims 31-32 and 34-35 is further limited in size because, with the exception of one both of nucleotide positions 1177 and 1601, the sequences encompassed by those claims comprise the sequence of SEQ ID NO:1.

Finally, new claim 33 is further limited because it must encode the amino acid sequence of SEQ ID NO:4. Thus, the polynucleotide sequences of claim 33 include sequence comprising SEQ ID NO:2, as well as sequences degenerate to SEQ ID NO:2. Page 41 of the Synopsis of Application of Written Description Guidelines points out that degenerate sequences are supported by the disclosure of a reference DNA sequence

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

such as the instant SEQ ID NO:2. The Guidelines state that "a person of skill in the art could readily envision all the DNAs degenerate to [a single reference sequence] by using a genetic code table." *Id.* Thus, the disclosure of SEQ ID NO:2 is sufficient to show possession of the genus of claim 33.

Rejection under 35 U.S.C. § 112, First Paragraph, Enablement

The Office also rejects claim 1, alleging that it is not enabled. (Office Action at page 5.) Applicants traverse this rejection.

Applicants again note that claim 1 is amended to recite that the claimed polynucleotides encode polypeptides with FSAP activity. Thus, one of ordinary skill in the art may screen an encoded polypeptide for its ability to activate prourokinase or Factor VII, as Applicants' specification illustrates in Tables 1 and 2. As illustrated in Applicants' specification, at page 1, second and third paragraphs, this prourokinase assay is known in the art. Further, it is illustrated in articles made of record in this application, such as that by J. Römisch et al. in *Blood Coagulation and Fibrinolysis*, 10: 471-9, published in 1999. The "materials and methods" section of that publication provides a detailed procedure for performing this assay, and the assay is illustrated in a number of the figures of the paper. (See Römisch et al. at page 472, "Quantitation of FVII activation," and at page 475, Figures 3-5.) The specification at that location provides one of ordinary skill in the art with scientific literature describing the assay. Moreover, it is a simple, routine assay. For example, as Römisch et al. illustrates, one may incubate the protease with Factor VII and other appropriate ingredients for a few minutes, stop the reaction, then use a commercial kit to quantify the active Factor VII.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

(*Id.*) Thus, no undue experimentation is needed to screen an FSAP mutant for FSAP activity.

Applicants also provide two monoclonal antibody-producing hybridoma strains, deposited in a public depository. The monoclonal antibodies from these strains can be used to identify FSAP mutants structurally, for example, following the procedure described beginning at page 18 of the specification. Such immunohistology screens are simple to perform and are routinely performed in the art. For example, an ELISA-type procedure can be used. Thus, no undue experimentation is needed to screen an FSAP mutant structurally.

In addition, determining a polynucleotide sequence to identify the base at positions 1177 and 1601 can be performed by automated DNA sequencing machines which have been in use for more than a decade and can analyze multiple samples at one time and read the sequence into a computer. A polypeptide sequence can also be determined by an automated Edman degradation procedure on a machine. Thus, no undue experimentation is required to characterize an FSAP mutant by its nucleotide sequence or by its polypeptide sequence.

The Office contends that it is not routine in the art to screen for multiple substitutions or modifications of a polynucleotide sequence. (Office Action at page 6, bridging to page 7.) However, techniques and assay systems are known and available in the art for doing just such screens. For example, the polymerase chain reaction (PCR) can be used to introduce multiple substitutions at either defined or random locations. All that is necessary is to use a primer encompassing a desired mutant nucleotide, or a stretch of partially randomized sequence. Such primers are made

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

routinely by machines in an automated process, while PCR is also a naturally automated procedure. Thus, no undue experimentation is required to make a number of FSAP mutants according to the claims. Second, it is routine in the art to use so-called microarrays to conduct monoclonal antibody screens on up to hundreds of samples at one time. A protein activity screen can also be tailored to test a number of samples at one time. Thus, screening number of FSAP mutants does not require undue experimentation because this process is currently amenable to simple automation.

Therefore, one of ordinary skill in the art can identify and characterize the claimed sequences and can use them as guided by the specification without undue experimentation because all of the steps needed are known in the art or provided in the specification.

Applicants also note that even if the experimentation needed to make and use the claimed sequences were lengthy or complex, this alone does not make that experimentation "undue." M.P.E.P. §§ 2164.01 and 2164.06; *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). "[A] considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Id.*

For all of the above reasons, Applicants request the withdrawal of this rejection.

Rejection under 35 U.S.C. § 112, Second Paragraph

Finally, the Office rejects claim 1 as allegedly indefinite, and contends that the location of positions 1177 and 1601 should be defined as the nucleotides located at positions 1177 and 1601 of SEQ ID NO:1. (Office Action at page 8.)

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

Applicants note that one of ordinary skill in the art would understand how to locate those positions based on the guidance provided by the specification. Indeed, according to M.P.E.P. § 2173.02, definiteness should be analyzed from the context of the application as a whole. Nevertheless, solely to speed prosecution, Applicants have amended claim 1, rendering this rejection moot.

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of claims 1-2 and 30-36.

Please grant all extensions of time required to enter this response and charge any required fees that are not found herewith to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

Dated: September 10, 2003

By: _____
Elizabeth A. Doherty
Reg. No. 50,894

Attachments: **Replacement Abstract**

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com